DISSERTATION

ON

A STUDY ON PROFILE OF SNAKE BITE INDUCED ACUTE KIDNEY INJURY AND OUTCOME

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CERTIFICATE

This is to certify that dissertation entitled **"A study on Profile of Snake Bite Induced Acute Kidney Injury and Outcome"** submitted by **Dr.R.Bathrinarayanan** to the faculty of General Medicine, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in the partial fulfillment of the requirement of M.D Degree - Branch I (General Medicine) is a bonafide research work carried out by him under my direct supervision and guidance.

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CONTENTS

INTRODUCTION

Snakes are fascinating part of nature. Their colour, movement and secret habits make them more mysterious. India is home to some of the most poisonous snakes in the world, most of which are found in rural areas. [1]

Snake bites cause substantial mortality and morbidity in India. A large proportion of snake bites occur when people are working barefoot in the fields, or while walking at night or early morning through fields or along roads. [2]

Superstitions, wrong practices, misconceptions [3,4] handicap doctors who care primary attention. [5]

Of 3000 species of snakes known to world, in India, we have around 216 species, out of which 52 are known to be poisonous. [6] Our venomous species belong to two major families: Elapidae, Viperidae.

We observe Acute Renal Failure / Acute Kidney Injury in majority of the cases. The gravity, spectrum and the outcome varies. Our study is to analyze Acute Renal Failure / Acute Kidney Injury in snake bite and to analyze various factors, influencing the outcome.

AIMS OF THE STUDY

1. To analyze the species causing Acute Kidney Injury.
2. To analyze the various risk factors associated with adverse outcome in patients with Acute Kidney Injury.
3. To correlate the association of treatment delay and outcome of Acute Kidney Injury.
4. To correlate the outcome of kidney injury with treatment modalities.
5. To analyze the autopsy findings of Acute Kidney Injury.

REVIEW OF LITERATURE

EPIDEMIOLOGY OF VENOMOUS SNAKES AND SNAKE BITE INDUCED ACUTE KIDNEY INJURY:

Snake bite poisoning is a preventable health hazard in tropics. Very extensive toxicological research still going on because of high incidence. It accounts for 100-150 deaths per day in India and the annual deaths per year is around 30,000.[6] It is a cause for major preventable death. In India, the highest incidence are in Tamil Nadu, West Bengal, Maharashtra, U.P and Kerala.[7]

Snake bites happen when the farmers work in field bare footed, unintentionally in a handful of foliage, rolling over the snake while asleep, while working in other plantation and in snake handlers.[8] Males are bitten most often than females[9] with majority of bite being on the lower extremities.[10]

Majority of victim initially are treated by traditional snake bite healers. Death often occurs even before the patient reaches hospital.[11] The use of protective foot wear, long trousers and lighting at night could reduce the incidence of snake bites. Effective rodent control could also help. [12]

Poisonous snakes prevalent in India belong to 3 families. [13] They are:

1) Elapidae: includes Cobras and Krait – Neurotoxic. Renal involvement is less common in victims bitten from members of this family.
2) Viperidae: Russell viper and saw scale viper – Vasculotoxic.
3) Sea snake: Myotoxic.

Renal involvement has been associated with bites from last two families. [14], [15]

COBRAS:

The two species of Cobras found in India [16] are common Cobra (Nalla Pambu) [17] and King Cobra (Raja Nagam, Karu Nagam). [17] The Cobra has hood which on dorsal side often bears a double or single spectacle mark. It is distributed throughout India. King cobra is black in colour and has hood but no mark on it. They found in Himalayas, Bengal, Assam and Andaman Islands. [18]

KRAIT:

The two species of krait commonly found in India[16] are common Krait (Kattu Viriyan) [17] and Banded Krait (Pattai Kattu Viriyan). [17] The common Krait has steel blue or black with white bars on the back. It is distributed through out India. [18] Banded krait is jet black with yellow stripes on its back. They found in Bengal, Assam, Bihar, Orissa, Madhya Pradesh, Andhra Pradesh and Uttar Pradesh. [18]

VIPER:

The two species of viper that are commonly found in India [16] are Russell viper (Kannadi Viriyan)[17] and Saw scale viper (Surruttai Viriyan).[17] Russell viper has a triangular head with V shaped mark pointing forwards. It has a white body with dark semilunar spots. It is seen in Maharashtra, Punjab, Rajasthan, Tamil Nadu and Andhra Pradesh. Saw scaled viper has many white lines on each flank of the back, with diamond shaped areas between the two lines. It has white mark resembling an arrow over the head. It is seen in hills and plains throughout India. [18]

SNAKE VENOM:

The venom is a modified salivary secretion. The normal function of snake venom is to immobilize the prey and assist in digestion. The toxic component of snake venom is classified into 4 broad categories namely enzymes, polypeptides, glycoproteins and compounds of low molecular weight. They can also be classified as protein (90-95%) and non protein (5-10%) compounds. [19] It also contains Clostridia, Anaerobes and Gram negative bacilli. Since they cause septicemia, treatment with Tetanus Toxoid, Tetanus Immunoglobulin and metronidazole, gram positive and gram negative antibiotics is warranted.

Table 1: Compounds present in snake venom[60]

Enzymes	Phopholipase A2 (lecithinase), 5' nucleotidase, collagenase, L-amino acid oxidase, proteinases, hyualuronidase, acetylcholine esterase, phospholipase B, endopeptidase, Kininogenase, Factor X, prothrombing activating enzyme.
Non enzyme polypeptides	Polysynaptic (a) neurotoxin (α bungarotoxin and cobrotoxin), presynaptic (b) neurotoxin (β bungarotoxin, crotoxin, and taipoxin) cardiotoxin, crotamine.
Peptides	Pyroglutamyl peptide
Nucleosides	Adenosine, guanosine, inosine
Lipids	Phospholipids, cholesterol
Amines	Histamine, serotonin, spermin
Metals	Copper, Zinc, Sodium, Magnesium

VARIOUS SNAKES, THEIR FATAL DOSE, QUANTITY OF VENOM INJECTED, AND TIME TO FATALITY [25] [60]

Snake	Fatal dose for humans	Average delivered dose per bite	Average Fatal Period
Indian Cobra	12mg	0.2g	8h
Common Krait	6mg	0.22g	18h
Russel's viper	15mg	0.15g	3days
Saw- scaled viper	8mg	0.13g	41days

The clinical presentation of a snake bite victim varies with the age and size of the patient, the species of snake, the number and location of the bites, the quantity and toxicity of the venom. Factors not contributing to outcome are size of the snake and time of bite (day/night). [8]

ENZYMES :[60]

Sl. No.	Enzymes	Actions
1	Acetylcholine Esterase	Catalysis and Hydrolysis of Acetylcholine
2	Arginine ester hydrolase	Bradykinin release, Interference with clotting
3	Hyaluronidase A[59]	Reduction of Collagen Viscosity
4	Phospholipase A	Un coupling of Oxidative Phosphorylation
5	Phospholipase B	Hydrolysis of lysophosphatides
6	Phophodiesterase	Inhibition of DNA, RNA, Arabinose derivatives
7	5' Nucleotidase	Specific Hydrolysis of Po4 Monoesterase which links with 5'position of DNA, RNA
8	L Amino acid Oxidase	Catalysis of Amino Acid
9	Thrombin like enzymes	Depression of Fibrinogen levels.
10	Proteolytic enzymes	Tissue destruction and bleeding
11	Collagenases	Collagen digestion

Arginine Esterase:

This enzyme is produced by snakes belonging to Crotalidae and viperidae. This enzyme has action similar to thrombin thereby causes coagulation and it releases bradykinin.

Phospholipase A:

It has a direct lytic effect, hemolytic effect and hydrolysis of phospholipase of RBC membrane, thereby causing sudden fall in BP. (13)

Cholinesterase:

It is an important enzyme of Cobra. It hydrolyses AcetylCholine into cholic acid and acetic acid. It has action similar to d-Tubocurarine and its effect is reversed by neostigmine.

Acetyl Choline – Cobra – Crotalidae:

It has direct action on heart and NeuroMuscular junction.

Proteinase :

Markedly present in Viper, Crotalidae. It cause tissue changes and destruction.

Anti coagulant effect:

It has anti coagulant effect due to proteolytic disintegration of Fibrinogen

Coagulant effect:

It had Coagulant effect by converting Prothrombin into Thrombin.

Non Enzymatic Components:

Haemorrhagins (HR-I, HR-II) – has direct action on endothelium with Procoagulant and Anticoagulant effects. It causes rapid haemorrhage, haemorrhages into visceral organs, vasoconstriction followed by vasodilatation of microvessels, haemorrhages into capillary bed and endothelial destruction.(59)

PATHOGENESIS OF ACUTE KIDNEY INJURY:

The exact pathogenesis of AKI following snake bite in not well established, due to the lack of a reproducible animal model. The factors that may contribute are. Direct Cytotoxicity, Bleeding, Hypotension, Circulatory collapse, Intravascular hemolysis, Disseminated Intravascular Coagulation and MicroAngiopathic Hemolytic Anemia (MAHA). [20]

Direct Nephrotoxicity:

Experimental studies with I^{125} -labeled E. *carinatus* venom [21] and the demonstration of venom antigen in human victims of snake bite using Enzyme-Linked Immuno Sorbent Assay technique have shown that the venom is excreted in the urine, without necessarily causing any damage to the kidney. [22] Urinary beta-N acetylglucosaminidase showed considerable change in patients bitten by *Russell's viper,* without DIC, indicating a direct toxic effect of venom on the kidney. [23]

In a study, the administration of a lethal dose of *Russell's viper* or E. *carinatus* venom to rhesus monkeys resulted in hemorrhages in the kidneys and other organs in all animals, and mild acute tubular necrosis in 20% of animals, within 24 hrs of envenomation. After a sub lethal venom dose, however, more than 50% of animals developed acute tubular necrosis, and fibrin thrombi were demonstrable in *50-75%* of glomeruli. [33] The histological findings and the

coagulation abnormalities observed in these animals were similar to those seen in human victims of snake bite. [14]

The strongest evidence supporting direct nephrotoxicity is a dose-dependent decrease in Inulin clearance and an increase in fractional excretion of sodium in the isolated perfused rat kidney, following *Russell's viper* envenomation. [24] However, this study did not include the morphological analysis of the perfused kidneys. To obtain further information about direct toxicity of *Russell's viper* venom (RVV) in renal tissue, Willinger et al [30] studied the combined functional and morphologic changes in isolated perfused rat kidney, complemented by studies in renal epithelial and mesangial cell cultures.

RVV administration induced changes in renal plasma flow, glomerular filtration rate; filtration fraction and tubular reabsorption of sodium were reduced, and fractional excretion of sodium and water showed an increase. Both oliguria and a subsequent polyuric phase could be demonstrated. On morphological analysis, the most prominent structural lesions were observed in the renal cortex. Extensive damage and loss of glomerular epithelial cells and endothelium was detected with only the basement membrane remaining. Ballooning and even rupture of glomerular capillaries could be seen.

Another prominent feature of RVV action is on renal cortex and other renal zones, concerned vessels with muscular walls (arteries, veins, arterioles, venules). The venom led to complete lysis of vascular smooth muscle cells leaving behind only the basement membrane. Varying degrees of epithelial injury occurred in all tubular segments.

In cell culture studies, RVV induced a complete disintegration of confluent mesangial cell layers at lower concentration. In epithelial cell cultures however, only extremely high doses of RVV led to microscopically discernible damage. Willinger et al, thus, demonstrated a direct dose dependent toxic effect of RVV on the isolated perfused rat kidney, directed primarily against glomerular and vascular structures and on cultured mesangial cells.

In addition myoglobinuria, sepsis, and hypersensitivity to venomous or anti-venomous protein may also contribute towards renal failure. Crescentic nephritis in patients bitten by puff adder has been attributed to hypersensitivity to antisnake venom. [26] Myoglobinuria generally occurs following sea snake envenomation, which results in necrosis of striated muscles and muscular paralysis. [27]

Hypotension:

Bleeding either into tissues or externally and loss of plasma into the bitten extremity can produce hypotension and circulatory collapse. This is caused by venom metalloproteinases that degrade basement membrane proteins surrounding the vessel wall, leading to loss of integrity. Hemorrhagic toxins have been isolated from venom of many snakes of Viperidae and Crotalidae families. [28] Hypotension is caused by release of Bradykinin. [29] Additionally, vasodilatation and increased capillary permeability, both as a result of direct and indirect effects of venom, can aggravate the circulatory disturbances of shock. [30] *Vipera palestinae* venom is thought to cause shock by depression of the medullary vasomotor center. [31] *Bitis arietans* causes hypotension by a combination of myocardial depression, arteriolar vasodilation and increased vascular permeability. Irrespective of the cause, hypotension and circulatory collapse set in motion a chain of hemodynamic disturbances, which are known to culminate in ischemic ARF.

Intravascular Hemolysis:

Another factor thought to have pathogenetic significance in snake-bite-induced ARF is intravascular hemolysis. [32] Hemolysis results from the action of phospholipase A_2 which is present in almost all snake venoms, and a basic protein called "direct lytic factor", found only in elapid venoms. [14] Phospholipase A_2 causes hemolysis by direct hydrolysis of red cell membrane phospholipids or indirectly via the production of the strongly hemolytic lysolecithin from plasma

lecithin. Evidence of intravascular hemolysis in the form of anemia, jaundice, reticulocytosis, raised plasma free hemoglobin, abnormal peripheral blood smear, and hemoglobinuria is present in about 50% of patients following bites by the *Russell's viper* and *E. carinatus.* [14] [34] In an experimental model using male Wistar rats, severe hemolysis was shown by increased plasma LDH levels, free hemoglobin and late presence of hemolysed red blood cell casts in renal tubules after infusion of venom of *Bothrops jararaca.* [35]

Some have even suggested that renal failure following snake bite should be considered an example of the hemolytic uremic syndrome. [36] However, while intravascular hemolysis is frequently observed, microangiopathic hemolysis as seen in hemolytic uremic syndrome is encountered only rarely. More over, more than 70-80% of patients with snake bite induced renal failure have only acute tubular necrosis and do not exhibit the glomerular and arteriolar changes characteristically associated with the hemolytic uremic syndrome. [37]

Disseminated intravascular coagulation:

The human hemostatic system is regulated via a number of critical interactions involving blood proteins, platelets, endothelial cells, and sub-endothelial structures. Snake venom proteins and peptides are known to activate or inactivate many of these interactions. Snake venoms, particularly those from the

viper and pit viper families, contain many proteins that interact with members of the coagulation cascade and the fibrinolytic pathway.

Russell's viper venom (RVV) contains a factor V-activating serine proteinase, [38] which has been separated from a factor X-activating protein, also present in this venom. The enzyme (RVV-V) is a single chain glycoprotein with a molecular weight of 26,100 possessing one glycosylation site near the carboxy terminus. RVV-V cleaves a single peptide bond to convert factor V to factor V_a (the activated clotting protein). *Russell's viper* venom also contains a potent activator of human coagulation factor X; this enzyme has been well characterized and is designated as RVV-X. [39] Factor X activators have also been isolated from *Bothrops atrox* and several other snake species. *Russell's viper* venom also activates factor IX by cleavage of a single peptide bond resulting in the formation of factor IX_a.

There are several different types of prothrombin activators in snake venom. The activity of members of group I is not influenced by components of the prothrombin activator complex (factor V_a, CaCl2 and phospholipid). Ecarin, from E. *carinatus* venom, is the most well studied member of this group. Group II activators resemble factor X_a and can cleave both peptide bonds in prothrombin, leading to active 2-chain thrombin. Their activity is strongly stimulated by phospholipids and factor V_a in the presence of $CaCl_2$. These enzymes are found

exclusively in the venoms of Australian elapid snakes, and the best studied one is from the tiger snake *(Notechis scutatus).* By contrast, activators in group III require only phospholipid and $CaCl_2$ for the activation of prothrombin. They do not require factor V_a, but appear to possess a co-factor that is tightly bound to the catalytic subunit that plays a similar role to factor V_a in prothrombin activation. This class of activator is also found in Australian elapids and is represented by the high molecular weight activator from Taipan venom *(Oxyuranus scutellatus).* [40]

Although thrombin has many activities, the ability of some snake venom enzymes to clot fibrinogen has resulted in these enzymes being called "thrombin-like". [41] These are widely distributed primarily in the venom of snakes from true vipers *(Bitis gabonica, Cerastes vipera)* and pit vipers *(Agkistrodon contortrix, Crotalus adamanteus, Bothrops atrox).* Snake venom fibrinogen clotting enzymes have been classified into several groups based on the rates of release of fibrinopeptides A and B from fibrinogen.

One mechanism of the anticoagulant action of snake venom proteins is attributed to the activation of protein C. Activated protein C degrades factors V_a and $VIII_a$ and therefore, has anticoagulant activity. Another mechanism of anticoagulation involves inhibition of blood coagulation factors IX and X by a venom protein(s) that binds to either or both. Finally, anticoagulation is also achieved through the action of snake venom phospholipases that degrade

phospholipids involved in the formation of complexes critical to the activation of the coagulation pathway. [42]

Direct-acting fibrinolytic enzymes have also been isolated from the venom of a number of North and South American snakes, including rattlesnakes and copperheads, and from elapids, including cobras and European vipers. [43] The venom fibrinolytic enzymes that have been characterized in detail are zinc metalloproteinases and may be classified as either α or β chain fibrin (ogen)ases. Snake venoms also contain a number of platelet active components, including those that cause platelet aggregation and those that inhibit platelet aggregation. [44]

The final coagulation disturbance depends upon the balance among the activity of procoagulant, anticoagulant, fibrinolytic and fibrinogenolytic components of injected venom. Disseminated intravascular coagulation (DIC) is a consistent feature in patients bitten by *Russell's viper, E. carinatus,* boomslang, and pit vipers. [45] The occurrence of DIC as a major hemostatic abnormality is well documented experimentally. Infusion of *Russell's viper* or *E. carinatus* venom into rhesus monkeys resulted in abnormal coagulation parameters suggestive of DIC within two hours of injection of a lethal dose of the venom, but these changes first occurred from a few hours to three weeks after sub-lethal envenomation. [46]

The presence of fibrin thrombi in the renal microvasculature and in the glomerular capillaries, and the findings of MAHA and thrombocytopenia in patients with cortical necrosis strongly suggest that DIC plays a major pathogenetic role in snake-bite induced cortical necrosis. [33] Snake venom initiates a chain reaction involving the coagulation, fibrinolytic, kinin and complement systems. Venom-induced alterations lead to vascular coagulation and to deposition of fibrin thrombi in blood vessels. These changes occur in patients as well as in experimental models. [33] [47] Intraglomerular fibrin deposition of lesser degree has been suspected as causing ATN via a temporary hemodynamic alteration.

The role of the above factors in causing ARF was shown in an experimental model by Burdmann et al. [35] They intravenously injected male Wistar rats with 0.4 mg/kg of *Bothrops jararaca* venom and produced functional and morphological changes similar to those observed in human snake-biteinduced ARF. There was an acute and significant decrease in the GFR, urine output, renal plasma flow and serum fibrinogen levels. There was intravascular hemolysis, as shown by a significant decrease in hematocrit, an increase in plasma LDH levels and free hemoglobin. Light and electron microscopy showed massive fibrin deposition in glomerular capillaries apart from proximal and distal tubular necrosis and red blood cell casts in renal tubules. In this model, ischemia related to glomerular coagulation and intravascular hemolysis were the most important pathogenetic factors causing a decrease in the GFR, although direct venom nephrotoxicity could not be excluded.

CLINICAL FEATURES:

Attempts should be made to determine whether a venomous snake bite has actually bitten the patient and if so, the severity of the bite.

Assessment of severity of envenomation[60]	
No Envenomation	Absence of local or systemic reactions, fang marks (+/-)
Mild Envenomation	Fang marks(+), moderate pain, minimal local edema (0-15cm) erythema(+), ecchymosis(+/-), No systemic reactions
Moderate Envenomation	Fang marks (+), severe pain, moderate local edema (15-30cm) erythema & ecchymosis (+), systemic weakness, sweating, syncompe, nausea, vomiting, anemia or thrombocytopenia.
Severe Envenomation	Fang marks (+), severe pain, severe local edema (>30cm) erythema & ecchymosis (+), hypotension, paresthesia, coma, pulmonary edema, respiratory failure.

Early symptom and signs:

Following the immediate pain of the bite, there may be increasing local pain (burning, bursting, and throbbing) at the site of the bite, local swelling that gradually extends proximally up the bitten limb and tender, painful enlargement of the regional lymph nodes draining the site of the bite. However, bites by kraits, sea snakes may be virtually painless and may cause negligible local swelling.

Regional Symptoms and Signs in the Bitten part:

Regional symptoms and signs include fang marks, local pain, local bleeding, bruising, lymphangitis, lymph node enlargement, inflammation, blistering, local infection, abscess formation and necrosis. Local swelling is a valuable sign of viper bite and the bite marks are deeper in viper bite. Local swelling occurs rarely with the Asian Cobra bite.

Generalised (systemic) Symptoms and Signs:

General:

It includes nausea, vomiting, abdominal pain, weakness, drowsiness and prostration. Fright reaction that develops in some patients should be differentiated from neurotoxicity.

Cardiovascular:

Cardiovascular symptoms seen mainly in patients bitten by Viper. It includes dizziness, faintness, collapse, hypotension, shock, cardiac arrhythmias, coronary vasoconstriction, pulmonary edema and cardiac arrest.

Neurolological:

Neurological symptoms seen mainly in patients bitten by snakes belonging to Elapidae. It includes drowsiness, paraestheiae, abnormalities of taste and smell, heavy eyelids, ptosis, external opthalmoplegia, paralysis of facial muscles, palatal and pharyngeal paralysis, flaccid limb paralysis, respiratory muscle paralysis, convulsions, coma, total body paralysis may last 3-5 days and takes weeks to resolve completely. Due to difficulty in swallowing secretions, patient may develop pulmonary aspiration sequelae – sub acute phase.

Muscular Breakdown:

It is seen in patients bitten by sea snake. Patient develops generalized pain, stiffness, tenderness of muscles, trismus, myoglobinuria, hyperkalemia, cardiac arrest and acute renal failure.

Renal:

Renal symptoms develop in patients bitten by snakes of Viperidae and hydrophidae family.[27] Patient manifest with loin pain, hematuria, hemoglobinuria, myoglobinuria, oliguria/anuria, symptoms of uremia (nausea, acidotic breathing, pleurisy). Ischemia (due to hypotension and DIC, [49] [50] nephrotoxic effect of venom, pigment nephropathy associated with rhabdomyolysis and intravascular hemolysis [14] [33] [37] leading to the development of acute tubular necrosis, bilateral cortical necrosis and renal failure commonly seen with Russell's viper. [14] [33]

Hemorrhage and Hemotoxicity:

It is seen in viper bite. Patient develop bleeding from recent wounds including fang marks, venepuncture sites etc. and from old partly healed wounds. Spontaneous systemic bleeding from gums, epistaxis, bleeding into tears, hemoptysis, hemetemesis, hemobilia, rectal bleeding or malena, hematuria, vaginal bleeding, bleeding into the skin (petechiae, purpura, ecchymoses) and mucosae (e.g., conjunctivae), intracranial hemorrhage, meningism from subarachnoid hemorrhage, lateralizing signs, or coma from cerebral hemorrhage and Acute Kidney Injury. [48] [49] Some patient show fragmented RBCs in Peripheral smear due to Intra Vascular Hemolysis (MAHA). [36]

Endocrine (Acute Pituitary / Adrenal insufficiency): (Russell's viper)

In acute phase, patient develops shock and hypoglycemia. In chronic phase (months to years after bite), some patient develops weakness, loss of secondary sexual hair, amenorrhoea, testicular atrophy, hypothyroids, hypopituitarism.

Long Term Complications:

At the site of bite, loss of tissue by sloughing or surgical debridement, results in chronic ulceration, infection, osteomyelitis, arthritis may persist causing severe physical disability. Malignant transformation may occur in skin ulcers after a number of years.

Chronic renal failure occurring after bilateral cortical necrosis and chronic Panhypopituitarism / Diabetes insipidus seen after Russell's viper bites. Chronic neurological deficits in patients who survive intracranial hemorrhages.

RENAL HISTOLOGY:

Renal histology shows predominantly either acute tubular or cortical necrosis. A number of glomerular changes have been described but their significance is not known.

Acute Tubular Necrosis:

Acute tubular necrosis is the predominant lesion seen in 70-80% of patients with ARF. [14] [33] On light microscopy, the tubules appear dilated and lined by flattened epithelium. Severe cases exhibit cell necrosis and desquamation of necrotic cells from the basement membrane. Hyaline, granular or, pigment casts are seen in tubular lumina. Varying degrees of interstitial edema, hemorrhage, and inflammatory cell infiltration are present. Later biopsies reveal regenerating tubular epithelium. Intrarenal blood vessels are usually unaffected.

On ultrastructural examination, proximal tubules show dense intra-cytoplasmic bodies representing degenerating organelles or protein resorption droplets. Small areas of basement membrane are denuded. Distal tubular cells have a dilated endoplasmic reticulum and many degenerating organelles. Apoptosis is a prominent feature in the distal tubules, indicating a high cell turnover. In the interstitium, fibroblasts appear active, with increased numbers of organelles and cytoplasmic processes. Mast cells and eosinophils show both granulated and partially degranulated forms. [51]

Although the blood vessels appear normal under light microscopy, ultrastructural abnormalities are notable in both large and small caliber vessels. [51] Medullary vessels are severely affected, with markedly swollen, focally necrotic, endothelial cells obliterating the lumen. Smooth-muscle cells show cytoplasmic vacuoles, which are empty or are filled with granular material. The severe vascular lesions, distal tubular apoptosis, and presence of mast cells, eosinophils, and active fibroblasts in the interstitium are features that have not been observed in acute tubular necrosis from other causes. [51]

Acute Cortical Necrosis

Bilateral diffuse or patchy cortical necrosis has been observed following bites by E. *carinatus.* Cortical necrosis appears to be more common among Indian patients than among patients in Thailand, for unknown reasons. [49] The presence of fibrin thrombi in the arterioles is a prominent feature in these patients. A narrow subcapsular rim of cortex often escapes necrosis. The area underlying this, however, shows necrosis of glomerular as well as tubular elements. The necrotic zone is often bordered by an area of hyperemia and leukocytic infiltration. Calcification of necrotic areas may occur at a later stage. Varying numbers of glomeruli are spared in patients with patchy cortical necrosis. With healing, fibroblastic proliferation and organization of thrombi are seen. Renal ultrastructure in cortical necrosis following *Russell's viper* bite has been studied in only two patients. [52] In one patient, the biopsy taken 10 days after the bite showed

glomeruli with collapsed capillary basement membrane, and denuded foot processes. No viable endothelial or mesangial cell could be identified, but swollen rounded cells, possibly of endothelial origin, were seen in some capillary lumina. Endothelial swelling of small arterioles and necrosis of peritubular capillaries were also seen. The tubular basement membrane was intact, but the epithelium showed degenerative changes. In the second patient, the biopsy was done 31 days after envenomation. In this patient, the urinary space contained unidentified cells with large cytoplasmic vacuoles. The tubular basement membrane was thickened, and the cortical tubules were lined by flattened epithelium, with large nuclei and a dilated endoplasmic reticulum. Fibroblastic proliferation was seen in the interstitium.

Glomerular Lesions

Whether or not specific glomerular lesions really occur is still controversial. Sant and Purandare [53] reported a "proliferative glomerulonephritis" in patients bitten by E. *carinatus.* Later, Seedat et al [26] reported two patients with crescentic glomerulonephritis, following puff adder bites, presenting as ARF. Because renal lesions of proliferative nephritis with crescents had developed with in 24-48 hours, these workers ascribed these lesions to an allergic reaction to snake venom. Sitprija and Boonpucknavig [54] described two patients with crescentic glomerulonephritis after *Russell's viper* bites. In another study of 38 patients bitten by the green pit viper or *Russell's viper,* the authors observed

thickening of the mesangial areas and mild mesangial proliferation in most of their patients, and diffuse glomerular hypercellularity (ascribed to marked mesangial proliferation) in two patients. Other glomerular changes observed are ballooning of capillaries, endothelial swelling, mesangiolysis and splitting of the glomerular basement membrane; however, the significance of these is difficult to ascertain. [55] Immunofluorescence microscopy showed IgM, C3, and fibrin deposits. [54] In occasional instances, a diffuse and intense mononuclear cell infiltrate has been noted in the interstitium, suggesting the occurrence of an acute interstitial nephritis. [56]

MANAGEMENT:

First aid treatment is carried out immediately after the bite either by the victim, or by any one else. The methods such as cauterization, incision / excision, suction by mouth, vacuum pumps, chemical application, cryotherapy and electric shock have been rejected. Application of bandage and tourniquet is not advised because of improper techniques, increased local effect of venom if brought late and ineffectiveness of the bandage, if the bitten limb is mobilized. Limb should be splinted after bite. Upper limb should be splinted in gravity neutral position at the level of heart. [57]

After the patient reached the hospital, rapid clinical assessment should be done regarding airway, breathing and circulation. Level of consciousness should be assessed. Urgent intervention should be done when the patient presents with profound shock, terminal respiratory failure, cardiac arrest precipitated by hyperkalemia, septicemia and renal failure.

Wounds should be cleaned, and administration of tetanus toxoid or tetanus immune globulin should be considered for under immunized or non-immunized patients. Patients should be given intravenous fluid, and venous blood should be drawn from an unaffected extremity in a small, clean, dry glass vessel. Leave the blood undisturbed for 20 minutes at room temperature and tilt the vessel once and the blood is still unclotted, conforms that coagulopathy and the biting species is viperine and rules out elapid bite.[61] The blood should be sent for Complete Blood Count, Peripheral Smear, Liver Function Test, Blood Urea, Serum Creatinine, CPK and ABG.[62]

Neutrophilia is seen in systemic envenomation. There is hemoconcentration due to capillary permeability and reduced platelets due to viper bite. Hematocrit is decreased due to blood loss or intravascular hemolysis. Peripheral smear shows fragmented RBC's when there is MAHA and the plasma is pinkish / brownish when there is hemoglobinemia and myoglobinemia respectively.

When renal failure develops, there is acidosis and blood urea, serum creatinine are elevated. Urine shows proteinuria and hematuria. When there is intravascular hemolysis, urine shows blackish urine. ECG shows evidence of hyperkalemia, ST-T changes, AV block. Chest X-ray shows features of pulmonary edema, pneumonia, pulmonary patchy opacities due to alveolar hemorrhages due to viper bite. Immunodiagnosis by ELISA identifies the species of snake correctly. It is not available in India. [8]

ANTI VENOM TREATMENT:

Anti venom is Immunoglobulin (enzyme refined Fab2 fragment of IgG) purified from serum or plasma of a horse or sheep that has been immunised with venoms of one or more species of snakes. In India, only polyvalent ASV is available and it neutralizes venom of four important snakes in India namely Indian cobra, Common krait, Russell viper and saw scaled viper. Though many researches, preparing ASV by human recombinant DNA technology is still unsuccessful.

Indications for ASV:

It is safe and desirable to wait for clear evidence of systemic poisoning to emerge before giving antivenom because of risk of untoward reactions. Allergic reactions known to occur in 15% of patients, although fatal anaphylaxis rarely occurs. Skin test with horse serum is a matter of controversy because it delays

therapy, has itself caused anaphylaxis and serum sickness and has been demonstrated to have a 10 to 36% false-negative rate and a 33% false positive rate.

ASV is given when there are hemostatic abnormalities i.e., spontaneous systemic bleeding, prolonged 20 min WBCT, thrombocytopenia and elevated FDP or D-dimer; neurotoxic signs i.e., ptosis, external opthalmoplegia & paralysis; cardiovascular abnormalities i.e., hypotension, shock, heart failure and pulmonary edema; supporting lab evidence of systemic envenoming, generalized rhabdomyolysis, Acute renal failure and signs of local envenomation [58]. The local swelling should be severe, indicated by the speed of swelling, for ASV administration.

All the patients in whom ASV is indicated should receive it. Care should be taken in cases of previous ASV allergy and history of atopy. These patients should receive S/C adrenaline, IV anti histamines, steroids.

Doses and Administrations

The recommended initial dosages are 100 ml of ASV (10 vials) for adults and children for both elapid &viper bite. 1 ML of ASV neutralizes 0.6 Mg venom of cobra and russell's viper, 0.45 mg of krait and saw scaled viper. But in vivo this

calculation fails. We require 100-150ml of ASV for mild envenomation and 300-500ml of ASV for severe envenomation and repetition of doses is also required.

ASV is available in freeze dried and liquid form. It is stored at temp below 8 degree Celsius. [63] It retains its efficacy up to 5yrs. When the solution looks opaque, it should be discarded due to the precipitation of proteins.

Several anti snake venom preparations are available internationally. In India, ASV producers belong to both Public as well as Private sector. They are as follows:

Anti-Snake Venom Producers in India[60]	
Public Sector	**Private Sector**
Central Research Institute(CRI), Shimla Hills, Kasauli, HP	Serum Institute of India Ltd. (SII), Pune
Haffkine Biopharmaceutical company Ltd. (HBPCL), Mumbai	VINS Bioproducts Ltd., Hyderabad
King's Institute of Preventive Medicine (KIPM), Chennai	Biological E Ltd., Hyderabad
Bengal Chemicals and Pharmaceuticals Ltd., Kolkata	Bharat Serum and Vaccine Ltd.

ASV should be given as early as possible and when it is delayed more than 2 hrs it will not reverse the local effect of snake venom. Once initial dose (10 vials) has been administered over one hr, no further ASV is given for 6 hrs. [64]

20 WBCT test every 6 hrs will determine if additional dose of ASV is required. ASV may be repeated till the coagulation profile is corrected. But patients who continue to bleed briskly, initial dose of ASV repeated within 1 to 2 hrs. [8]

Methods of Administration:

It can be given as IV push at the rate of 2ml/min or it is diluted in 100 ml of normal saline and given over 1 hr. As the half life of Indian ASV is around 90hr, there is no requirement to extent the administration period. Local administration at the bitten site is not recommended. [60]

Response to ASV:

If adequate dose of ASV has been given then the patient feels better. Nausea, headache, generalised ache disappears. Spontaneous systemic bleeding stops in 15 to 30 min. Blood coagulability restored in 3 to 9hrs as measured by 20min WBCT. Shock improves in first 30 to 60 min [65] and arrythmias may resolve. Neurotoxic symptoms (Cobra) begin to improve as early as 30min. [66] Active hemolysis may cease within a few hrs and urine returns to normal.

ASV Reactions:

If patient develops allergy to ASV, they either present in the form of early anaphylactic reaction, pyrogenic reaction or late serum sickness like reactions. They are treated with antihistamines, adrenaline and steroids. (8)

COMPLICATIONS OF SNAKE VENOM & MANAGEMENT:

Hypotension and shock are treated with ASV, plasma expanders and vasoconstrictors. Russell's viper bite results in acute pituitary, adrenal insufficiency & responds to hydrocortisone. Hemostatic disturbances respond well to ASV. ASV is given to neutralise procoagulant and toxins. FFP, cryoprecipitate, fresh whole blood are given to restore coagulability. (8)

Bitten limb nursed in most comfortable position, slightly elevated. Prophylactic antibiotics like penicillin and metronidazole should be given. If wound is incised use broad spectrum antibiotics. (8)

RENAL FAILURE is due to multi factorial causes. Early correction of shock & ASV is important to avoid ARF. Situations of oliguria where ARF not established, frusemide with fluid challenge or mannitol challenge can be tried. MC cause of ARF is ATN and has good prognosis. 10% of cases develop ACN & it is bad prognosis.

Indication for dialysis:

Patient is taken up for dialysis when his general condition deteriorates due to hyperkalemia, pulmonary edema, severe acidosis and when the biochemical parameters are raised. In non oliguric renal failure, the decision is done based on raising biochemical parameters.

Hemodialysis is done in patients with normal hemodynamic status. Those who are hemodynamically unstable, Peritoneal dialysis is done. Patient with AKI recovers in 3 weeks. If the patient does not recover think of Cortical Necrosis and Biopsy is medial. Prognosis of patients with renal failure is very good and they recover with appropriate treatment. [67] Prognosis of patients with cortical necrosis is poor. [68] [69] [70] They go in for Chronic Kidney Disease.[14]

MATERIALS AND METHODS

The study was conducted in Thanjavur Medical College Hospital, Thanjavur, Tamilnadu and was conducted in the Department of Internal Medicine and Intensive Medical Care Unit. Study period extended from October 2007 to July 2008. It was a carefully selected study on patients developing Acute Kidney Injury following snake bite. Patients were selected on the basis of inclusion and exclusion criteria. Total number of 50 patients including both male and female were taken up for the study.

INCLUSION CRITERIA:

Patients with snake bite, developing Acute Kidney Injury.

EXCLUSION CRITERIA:

1) Known Hypertensive and on treatment.
2) Known Diabetic and on treatment
3) Chronic history of NSAID intake
4) Past history of renal disease.
5) Previous Ultrasonogram evidence of Chronic Kidney disease.
6) Contracted Kidneys by Abdominal Ultrasound.

DEFINITION OF ACUTE KIDNEY INJURY:

PROPOSED CLASSIFICATION OF ACUTE KIDNEY INJURY – MODIFIED RIFLE CRITERIA[71]		
STAGE	SERUM CREATININE CRITERIA	URINE OUTPUT CRITERIA
1(Risk)	Increase of ≥ 0.3mg / dL or 1.5 – 2 fold increase of the baseline.	< 0.5 ml / Kg / h > 6hr
2 (Injury)	Increase to 2 – 3 fold of the baseline	< 0.5 ml / Kg / h for > 12 hr
3 (Failure)	Increase to > 3 fold or serum creatinine ≥ 4 mg/dL with an acute rise of atleast 0.5mg/dL.	0.3ml/kg/hr for 24hr or anuria for 12hr.

STUDY PROTOCOL

History:

A detailed history was elicited for

-Age & gender

- Co-morbid diseases and concomitant drugs.

- Species of snake

- Site & time of bite

- Native treatment

- Treatment before Hospitalization

- Hematuria, hemetemesis, hemoptysis, bleeding gums and bleeding from the site of bite.

- History of reduced urine output, oliguria and anuria.

CLINICAL EXAMINATION: A thorough physical examination was done to look for local and systemic features of envenomation.

EVIDENCE FOR REGIONAL ENVENOMATION:

Site of snake bite is examined for presence of fang marks, cellulitis, bleeding from site of bite, local necrosis, blistering, gangrene, regional lymph node enlargement and evidence for compartment syndrome.

All Vital signs looked for.

EVIDENCE FOR SYSTEMIC ENVENOMATION:

Features of bleeding manifestations – gum bleeding, epistaxis, ecchymosis.

Features of Neuroparalysis

Azotemia / Uremic symptoms.

INVESTIGATIONS:

1. Complete Blood Count
2. Bleeding time
3. Clotting time
4. Urine Albumin, Sugar, Deposits including RBCs
5. Blood urea, serum creatinine, electrolytes
6. Electrocardiogram
7. USG abdomen
8. CT Brain for required cases.
9. Other investigations were taken based on the clinical status of the patient.

Patients underwent physical examination daily. Pulse rate, Blood pressure, Urine output, Respiratory rate and features of envenomation were monitored daily. Blood specimen was taken everyday till discharge or death to measure sodium, potassium, urea, creatinine, bleeding time, clotting time, platelets and for patients undergoing dialysis, pre-dialysis and post-dialysis Urea and Creatinine was measured for each cycle.

TREATMENT GIVEN:

1. Injection Tetanus Toxoid 0.5ml subcutaneous on admission.
2. Cleaning of the wound and area with soap and water.
3. IV line secured for fluids and ASV.
4. Specific treatment Inj ASV IV bolus and followed up doses depending upon the class of envenomation and biochemical parameters. Bite to ASV time noted.
5. Repeated doses of ASV based on signs of envenomation and biochemical parameters.
6. Maintenance of fluid volume, blood pressure.
7. Drugs Ampicillin, cefotaxime, metronidazole given in regular dose and dose adjustment has done depending upon renal status.
8. Observation.

9. Patient having evidence of Acute Kidney Injury were identified.
10. Dialysis program based on volume overload, urine output status, clinical azotemia, uremic symptoms and renal biochemical parameters.
11. Repeated PD/HD depending upon the renal improvement.

RESULTS AND ANALYSIS

In our study of 50 patients, Age of the patient ranges from 12-65yrs and proportion of patients in each age group is as follows:

AGE	11-20	21-30	31-40	41-50	51-60	61-70
No.	8 (16%)	14 (28%)	7 (14%)	9 (18%)	6 (12%)	6 (12%)

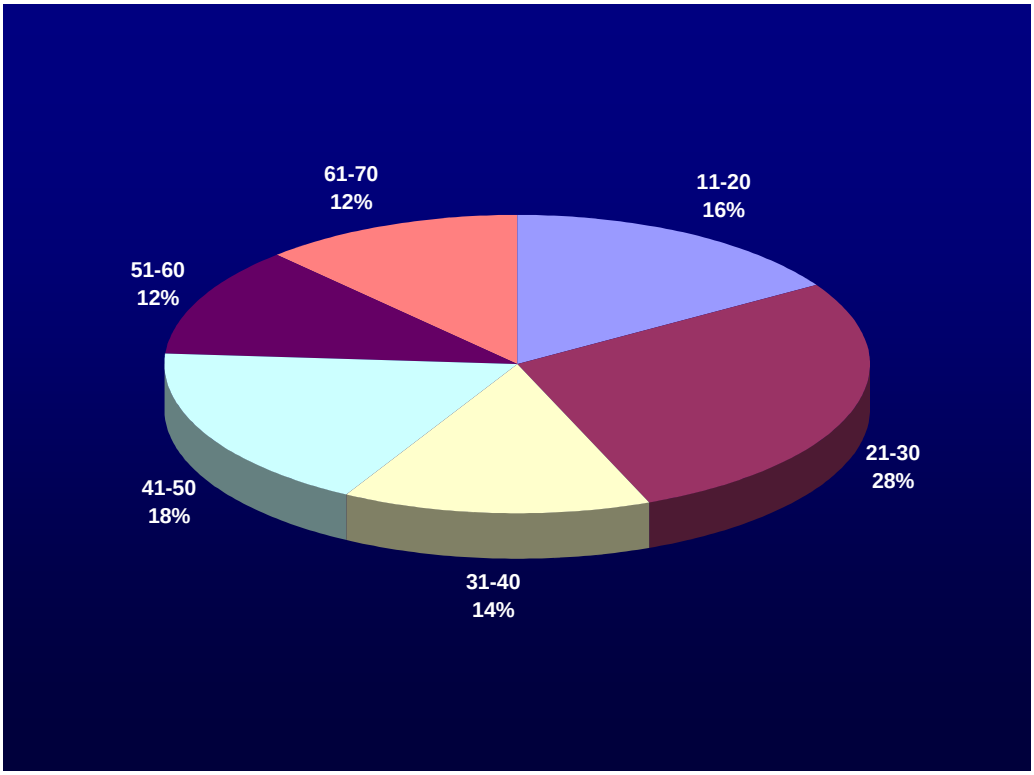

Figure-1

In our study of 50 patients, 27 were male and 23 were female.

Sex	Male	Female
No.	27 (54%)	23 (46%)

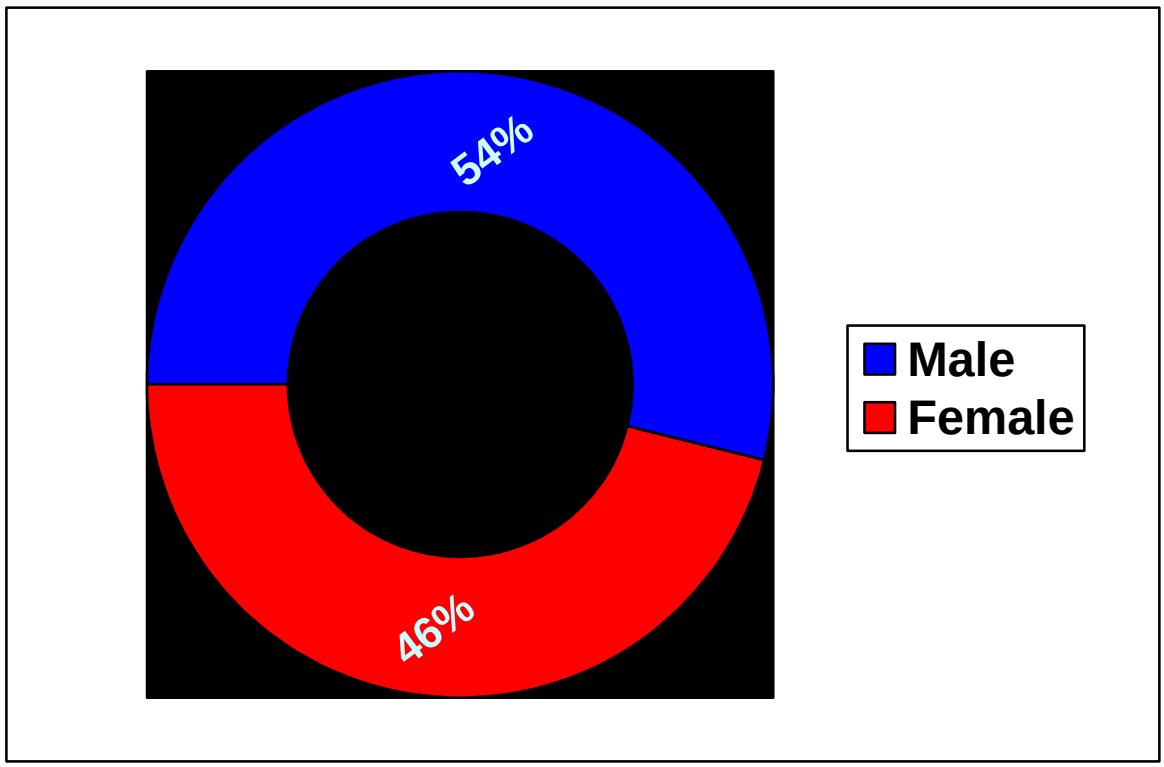

Figure -2

In our study of 50 patients, who developed Acute Kidney Injury, Species of snake was identified as viper in 30 patients (22 patients Russell Viper and 8 patients saw scaled Viper); of the remaining 20 patients species could not be identified.

Species	No.
Russell Viper	22 (44%)
Saw Scaled Viper	8 (16%)
Unidentified	20 (40%)

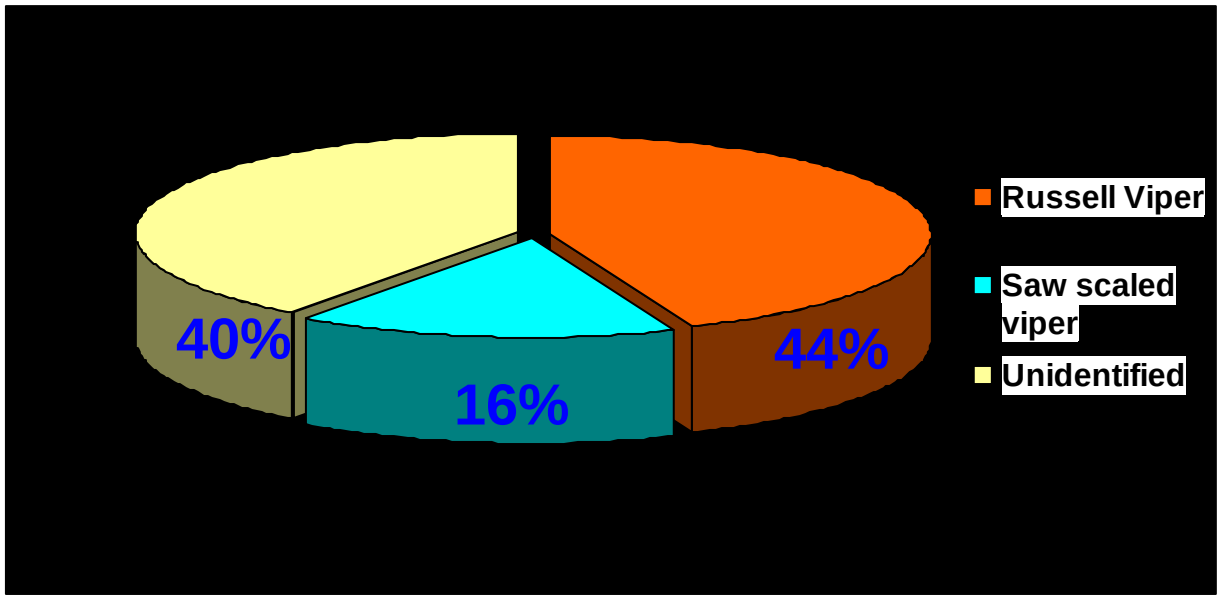

Figure-3

Out of the 50 patients in this study, 31 patients survived and 19 patients died. Mortality rate in our study – 38%.

Patients	Died	Survived
No.	19 (38%)	31 (62%)

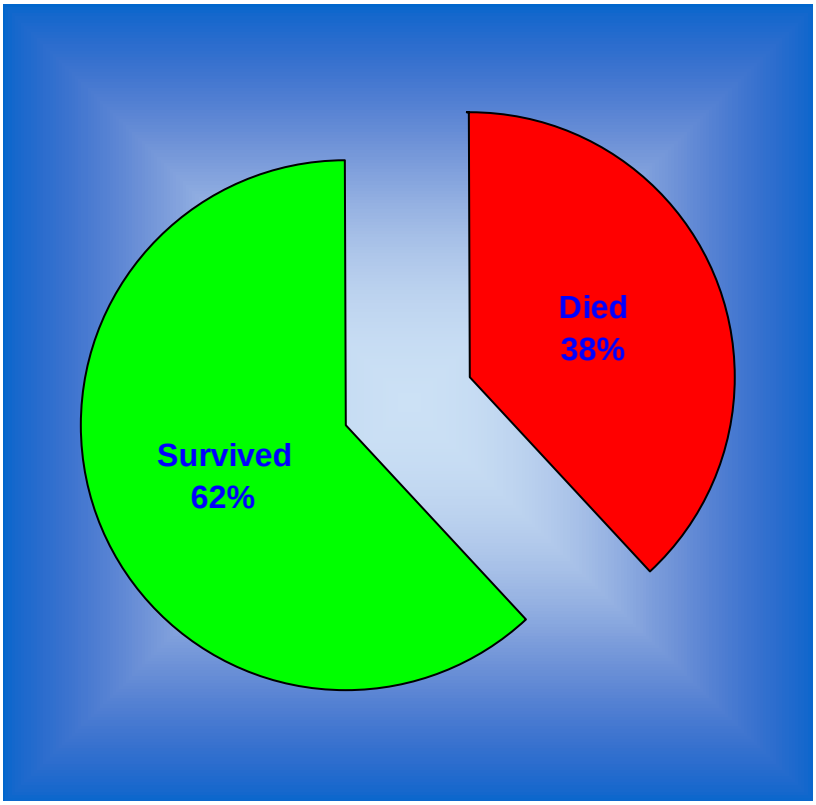

Figure - 4

In this study of 50 patients, 27 were male and 23 were female. Out of the 27 male patients, 17 survived and 10 died. Out of 23 female patients, 14 survived and 9 died.

Variables	Survived	Died
Male	17 (34%)	10 (20%)
Female	14 (28%)	9 (18%)

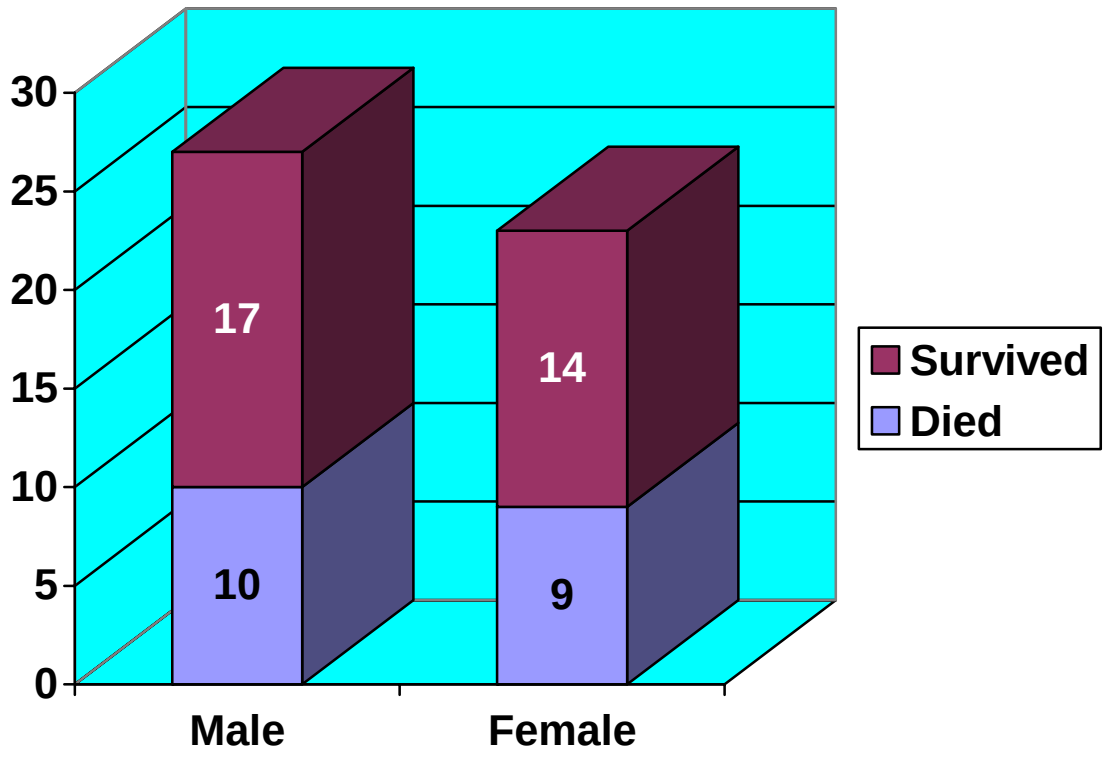

Figure-5

In our study of 50 patients with Acute Kidney Injury, 49 patients developed cellulitis. Out of the 49, 30 survived and 19 died.

	Survived	Died
Cellulitis	30 (60%)	19 (38%)
No Cellulitis	1 (2%)	0 (0%)

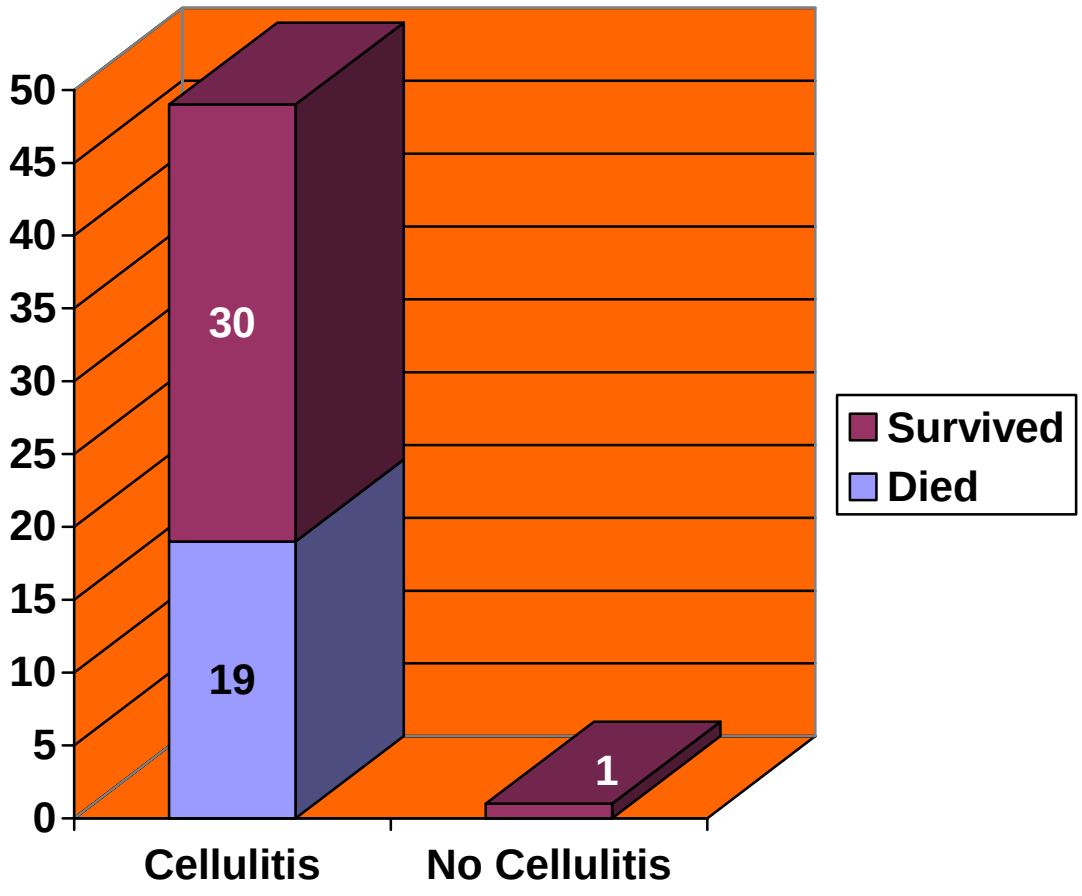

Figure-6

In this study of 50 patients with Acute Kidney Injury 9 patients had Bleeding Manifestations (Hematuria, Gum bleeding, Hemetemesis), out of which 7 died.

Variable	Survived	Died
Bleeding Manifestation	2 (4%)	7 (14%)
No Bleeding Manifestation	29 (58%)	12 (24%)

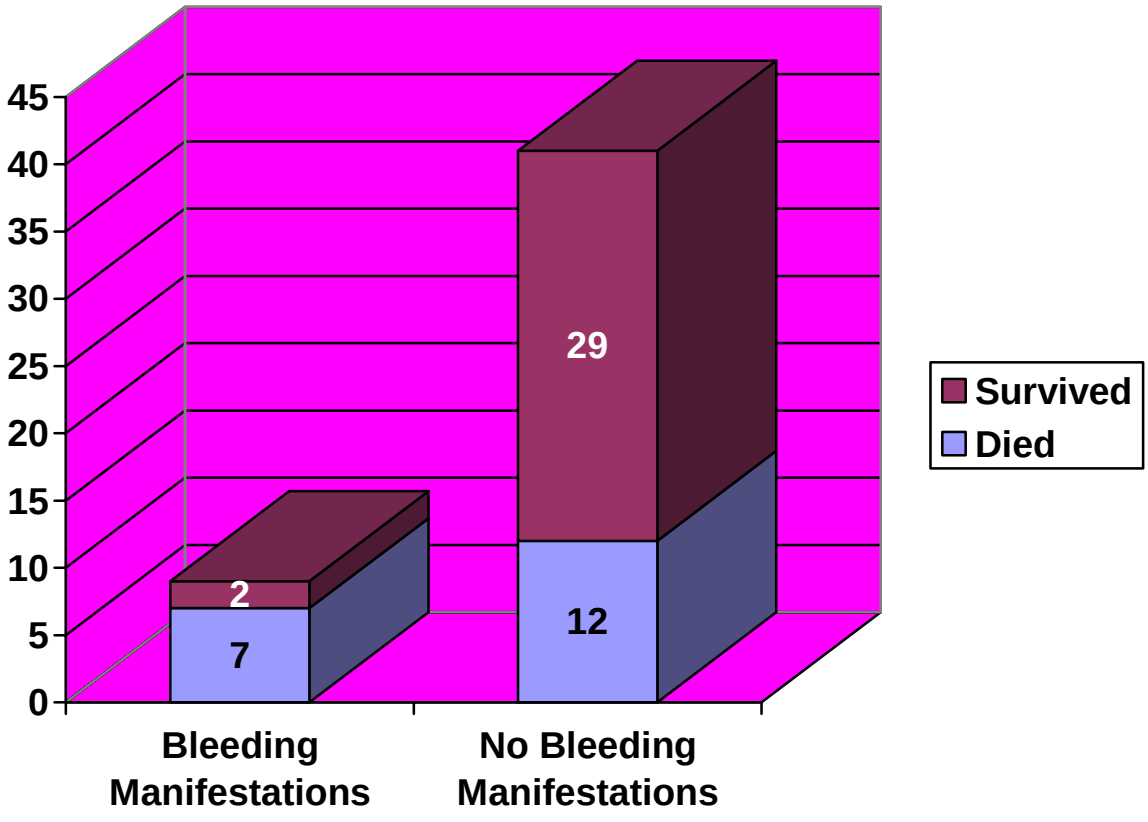

Figure-7

In our study of 50 patients with Acute Kidney Injury, 23 patients presented with hypotension (systolic <90 mmHg), out of the 23 patients, 8 survived and remaining15 died.

Variable	Survived	Died
Hypotension	8 (16%)	15 (30%)
Normal Blood Pressure	23 (46%)	4 (8%)

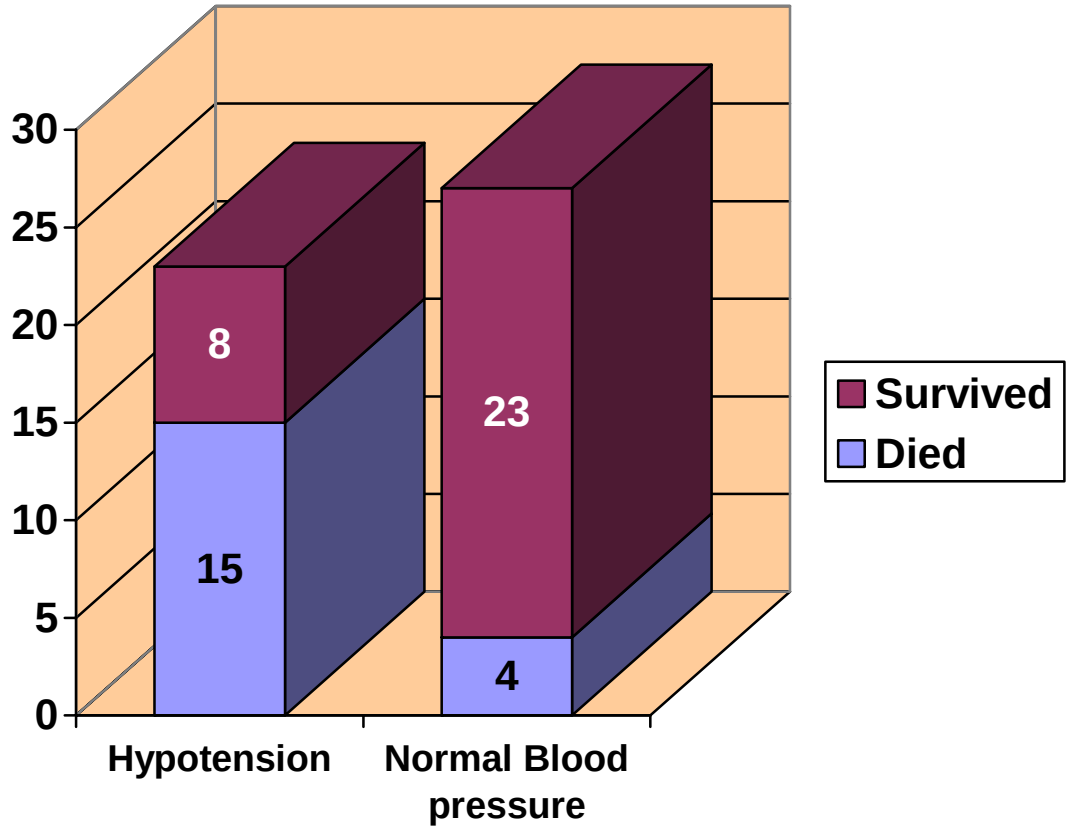

Figure-8

In our study of 50 patients with Acute Kidney Injury, 32 received early therapy (Bite to ASV time <6hrs) with Anti snake venom. Of the 32 who received ASV < 6hrs, 27 survived and 5 died. Of the remaining 18 who received ASV after 6hrs, only 4 survived.

Variable	Survived	Died
Bite to ASV > 6hrs	4 (8%)	14 (28%)
Bite to ASV <6hrs	27 (54%)	5 (10%)

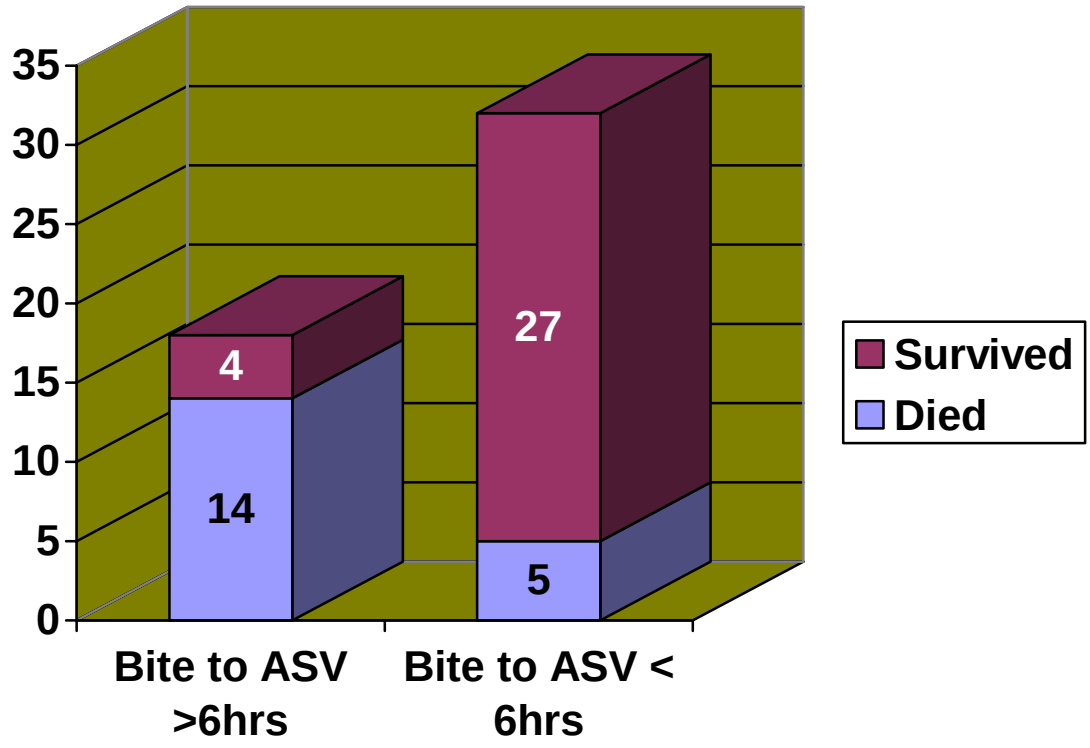

Figure-9

Out of the 50 patients in our study, 30 patients required dialysis and remaining 20 patients were treated conservatively. Peritoneal dialysis alone was done in 17 patients and both peritoneal and hemodialysis was done in 13 patients.

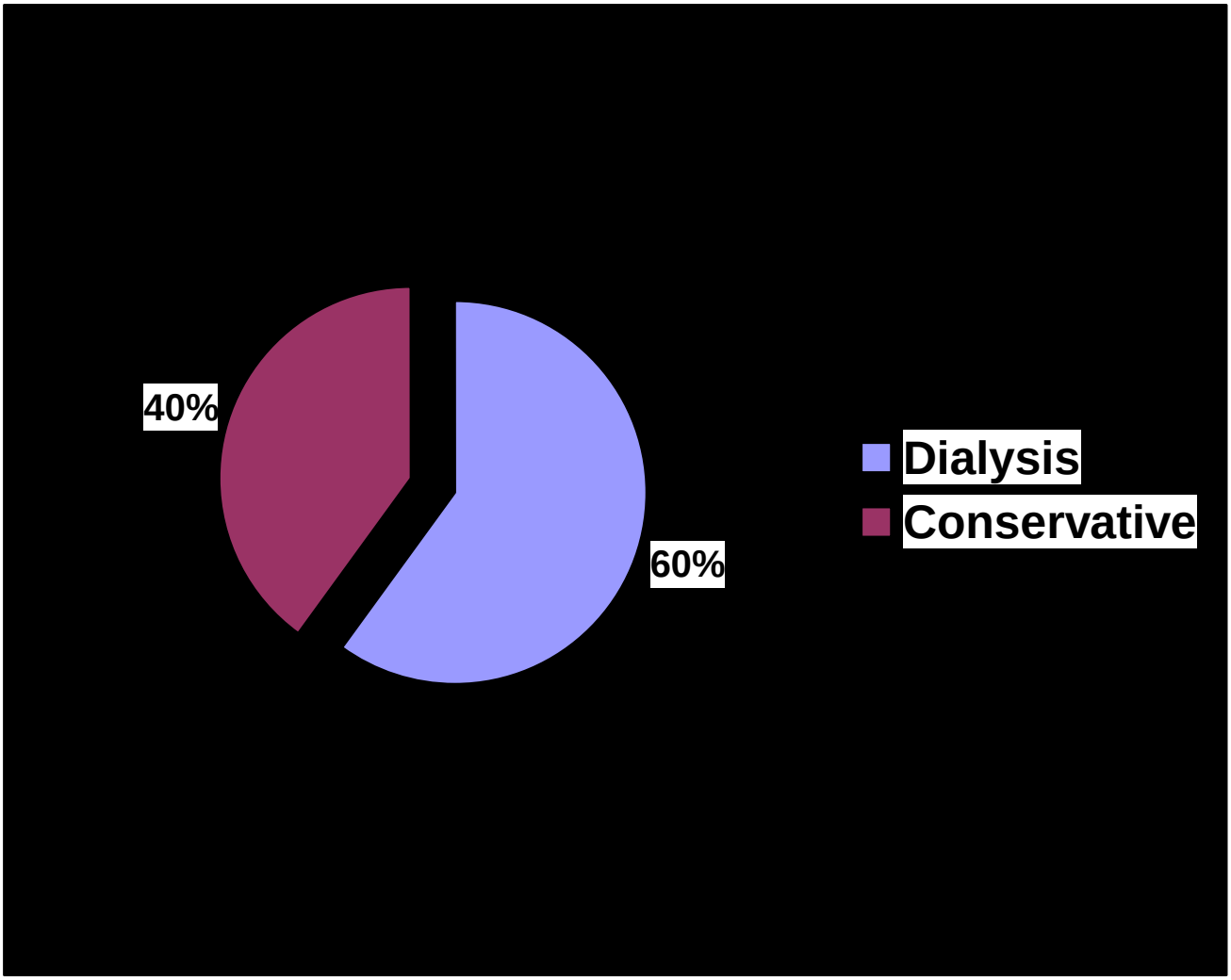

Figure-10

Out of 30 patients who required dialysis, repeated cycles (>2) were done in 11 patients. While others recovered with <2 cycles of dialysis.

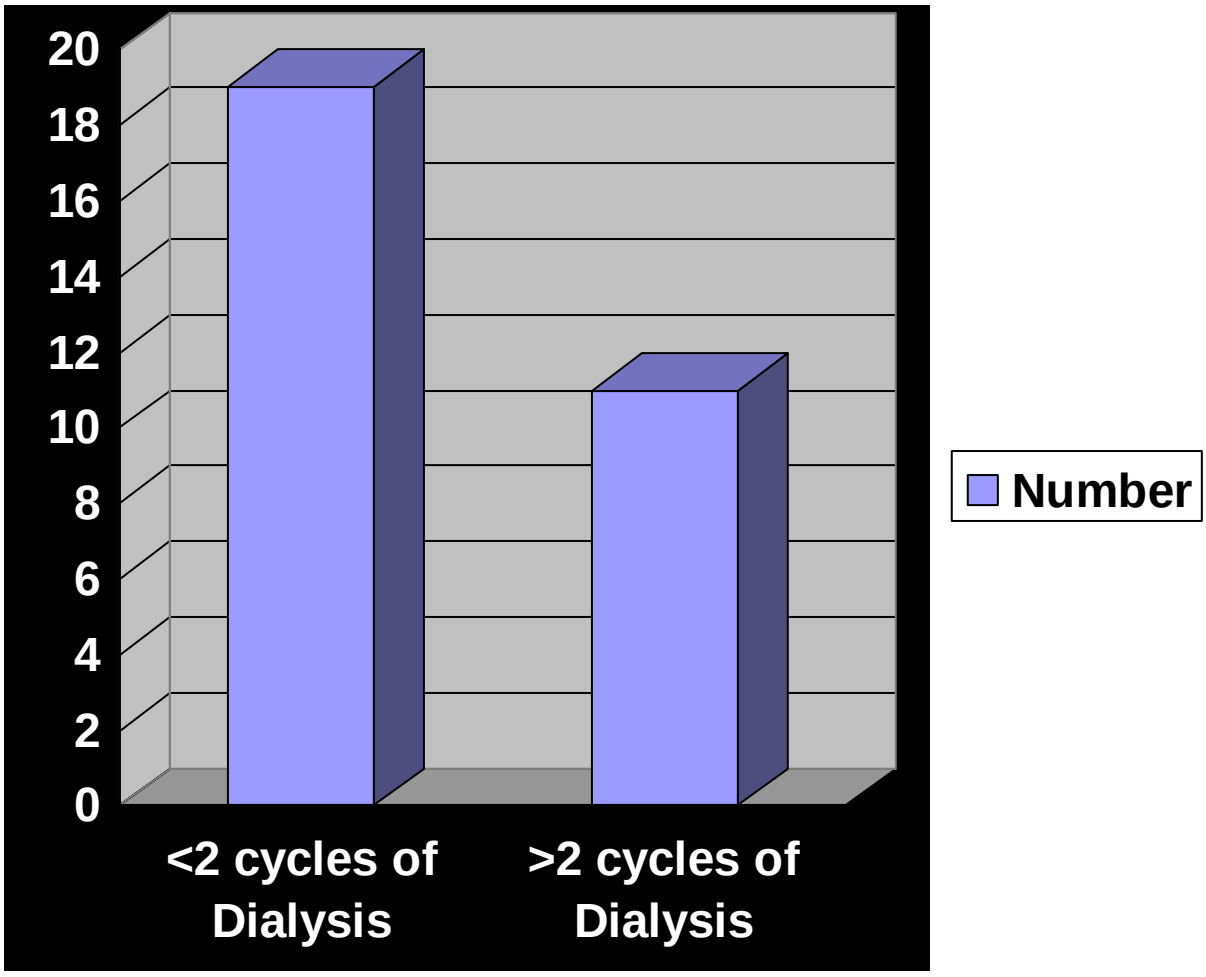

Figure-11

Out of 30 patients who required Dialysis (PD/HD), 23 patients survived and 7 patients died.

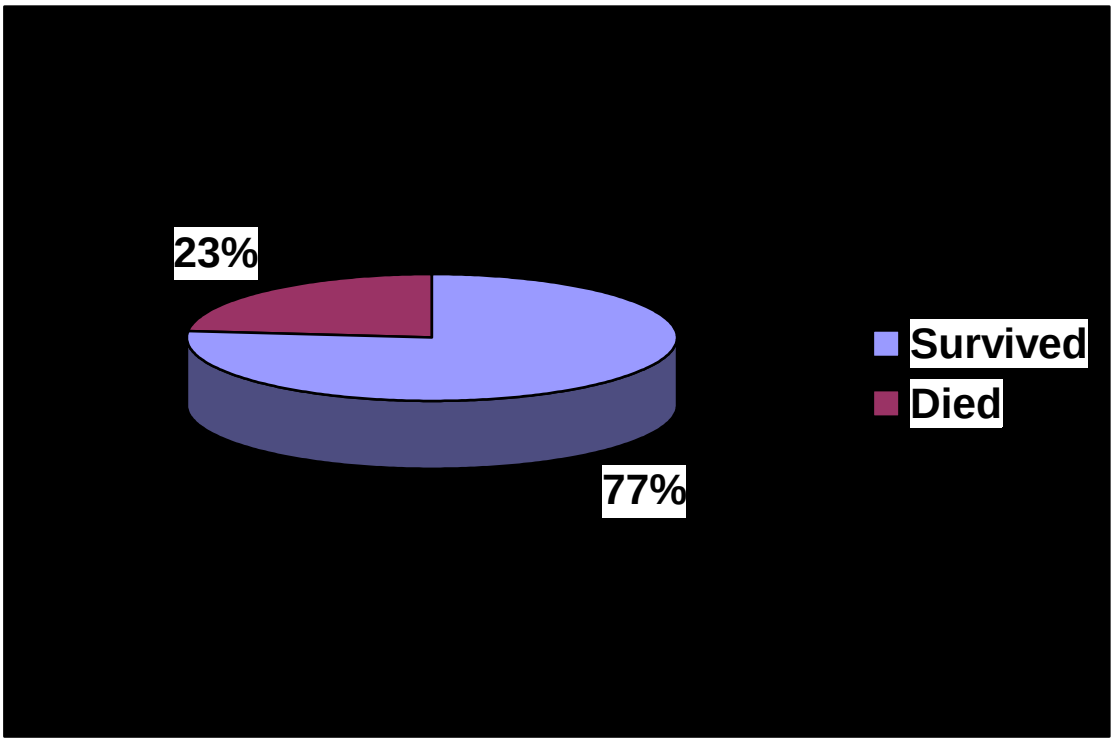

Figure-12

Out of 19 patients died, in autopsy, 4 had evidence of Cortical Necrosis and all had Bilateral Congested Kidneys.

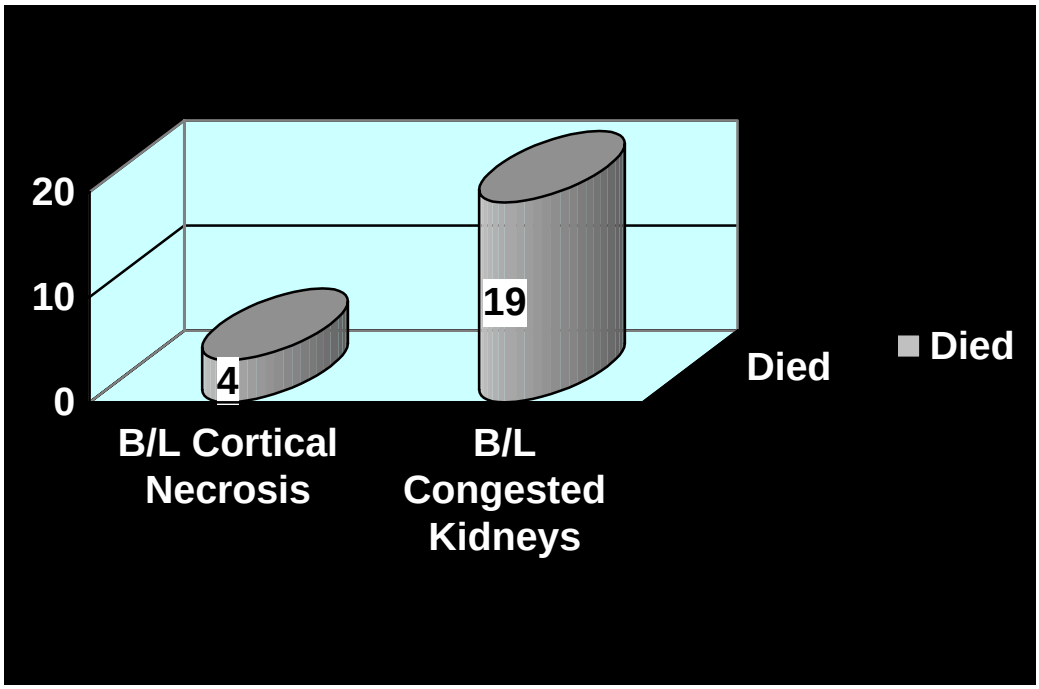

Figure-13

Analysis of results

The results were analyzed with Chi-square test.

a) In our study of 50 patients, most of the patients were in the age group of 21- 50yrs (60%)

By using the statistical methods, Age of the patient does not show any statistically significant relationship to mortality.

b) In our study of 50 patients, there was a nearly equal distribution of male (54%) and female (46%).

By using the statistical methods, Age of the patient does not show any statistically significant relationship to mortality.

c) In our study out of the 50 patients, species of snake was identified in 30(60%) of the patients. All of the 30 were identified are Vipers out of which 22 (44%) were Russell viper and 8 (16%) were saw scaled viper.

d) In our study of 50 patients, 31 patients survived and 19 patients died. The mortality rate was 38%.

Increased mortality in our study was not a direct mortality, other factors influence the mortality.

We assessed the various risk factors associated with adverse outcomes in patient with Acute Kidney Injury.

e) In our study of 50 patients, 49 (98%) patients in our study had Cellulitis, out of which 19(38%) died.

Using chi square test a p value of 1.00 obtained which shows that there was no statistically significant association between patients having Cellulitis and mortality.

f) In our study of 50 patients, 9 patients (18%) presented with bleeding manifestations out of which 7 died. Of the remaining 41 (82%) patients without bleeding manifestations, 12 patients died.

By using chi square test a p value of 0.018 was obtained which shows that there was a statistically significant relationship between the patients developing bleeding manifestations and mortality.

g) In our study of the 50 patients, 23 presented with hypotension out of which 15 died and 8 survived. Of the remaining 27, only 4 patients died.

By using chi square test a p value of <0.001 (very significant) was obtained. This shows that there was a strong statistically significance between hypotension and mortality.

h) In our study of 50 patients, 32 patients received early therapy (Bite to ASV < 6hrs) with polyvalent Anti Snake Venom out of which 5 died. Of the remaining 18 patients who received ASV>6hrs, 14 died and only 4 survived.

By using chi square test a p value of <0.001 (very significant) was obtained which shows a statistically significant association between early therapy with ASV and mortality.

Early therapy with ASV will reduce the mortality rate in patients with renal failure.

Of the various factors we studied statistically significant association have been found between hypotension, bleeding manifestation, early therapy with ASV and mortality.

i) In our study of 50 patients, 30 patients were treated with dialysis out of which only 7 died. Mortality rate in patients treated with dialysis is 14%.

j) Autopsy findings of the Kidney:

All patients had evidence of Renal involvement

All patients showed congested kidney, which may be parenchymal, and or vascular. 4 patients showed definite Autopsy evidence of Acute Cortical Necrosis.

DISCUSSION

PROFILE OF SNAKE BITE INDUCED ACUTE KIDNEY INJURY & OUTCOME

Inference 1:

This study shows statistical evidence that Age of the patient does not correlate with mortality.

The above inference is supported by the study done by **Ganesh Athappan et al.** [72]

Inference 2:

This study shows statistical evidence that Sex of the patient does not correlate with mortality.

The above inference is supported by the study done by **Ganesh Athappan et al.**[72]

Inference 3:

In our study, the most common species causing Acute Kidney Injury is Viper.

The above inference is supported by the studies of

Ganesh Athappan et al., [72] **N. Suchitra et al.,** [73] **Jin-Bor Chen et al.** [78] **and G. Ali et al.** [75]

Inference 4:

In our study, the mortality rate was 38%. Increased mortality rate in our study was not a direct mortality, other factor influence it. This is one inference in our study which does not correlate with the results of other studies.

Mortality rate in other studies:

Athappan G., Balaji MV et al –mortality rate 22.5% [72]

G.Ali, M.Kac, M.Kumar et al –mortality rate 25% [75]

Chugh et al –mortality rate 28.6% [14]

Inference 5:

In our study, all patients except one developed cellulites. This study shows statistical evidence that Cellulitis does not correlate with mortality.

The above inference is supported by

Athappan G., et al. [72]

Inference 6:

In our study, 9 patients developed bleeding manifestations. This study shows statistical evidence that Bleeding manifestations after snake bite correlate well with mortality.

The above inference is supported by

Athappan G. et al., [72] Suchitra N et al. [73] and Ali G. et al. [75]

Inference 7:

In our study, 23 patients developed hypotension. This study shows statistical evidence that Hypotension after snake bite correlate well with mortality.

The above inference is supported by

Athappan G. et al. [72] And Ali G. et al [75]

Inference 8:

In our study, 32 patients received ASV within 6hrs. This study shows statistical evidence that late therapy with ASV i.e., more than 6hrs is strongly associated with mortality.

The above inference is supported by

Athappan G. et al., [72] Ali G. et al., [75] Narvencar K. et al., [74] Mohammed A. Al Homrany et al., [76] Jin-Bor Chen et al., [78] Looareesuwan et al. [79] And Suchitra N. et al. [73]

Inference 9:

Early treatment in snake bite patients developing AKI with Dialysis (PD/HD) is associated with better outcome.

The above inference is supported by

Athappan G. et al., [72] and Kumbhalkar SD et al. [77]

Inference 10:

In our study, all patients who died in autopsy had evidence of renal involvement, with 4 patients had evidence of Cortical Necrosis.

The above inference is supported by

K. S. Chugh, B. K. Aikat et al [80]

CONCLUSION

1. Viper bite accounted for definite Acute Kidney Injury.
2. Major Risk factors linked with adverse outcome in Snake bite with Acute Kidney Injury
    a. Hypotension
    b. Bleeding manifestations
    c. Delayed specific therapy with ASV.
3. Age, Gender and Presence of Cellulitis does not influence the mortality in patients with Acute Kidney Injury.
4. Early therapy with Anti snake venom was associated with better outcome in terms of mortality.
5. Early institution of dialysis had definite favourable outcome in Acute Kidney Injury.
6. All patients with Acute Kidney Injury showed autopsy findings of renal involvement.

ABBREVIATION:

AKI	– Acute Kidney Injury
IMCU	– Intensive Medical Care Unit
UP	– Uttar Pradesh
BP	– Blood Pressure
PR	– Pulse Rate
HR	– Haemorrhagin
DIC	– Disseminated Intravascular Coagulation
MAHA	– Micro Angiopathic Hemolytic Anemia
RVV	– Russells' Viper Venom
ARF	– Acute Renal Failure
LDH	– Lactate De Hydrogenase
CaCl2	– Calcium Chloride
CPK	– Creatinine Phospho Kinase
CK	– Congested Kidney
ABG	– Arterial Blood Gas
ASV	– Anti Snake Venom
AV block	– Atrio Ventricular Block
DNA	– Deoxy Ribo Nucleic Acid
WBCT	– Whole Blood Clotting Time
FDP	– Fibrin Degradation Product
ATN	– Acute Tubular Necrosis
ACN	– Acute Cortical Necrosis.

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A Study On Profile of Snake Bite Induced Acute Kidney Injury & Outcome

Name Age Sex IP. No.

Occupation Date and Time of Admission

Address

Diagnosis:

Presenting Complaints:

- Species of snake
- Site & time of bite
- Native treatment
- Treatment before Hospitalization
- Hematuria, hemetemesis, hemoptysis, bleeding gums and bleeding from the site of bite.
- History of reduced urine output, oliguria and anuria
- Symptoms of local and systemic envenomation.

Past History:

- DM, HT, Chronic NSAID intake, chronic Kidney disease and Treatment

CLINICAL EXAMINATION:

EVIDENCE FOR REGIONAL ENVENOMATION:

□ Fang marks □ Cellulites □ Bleeding from site of bite

□ Local necrosis □Blistering □Gangrene

□Regional lymph node enlargement □ Evidence for compartment syndrome.

PR-

BP-

EVIDENCE FOR SYSTEMIC ENVENOMATION:

Features of bleeding manifestations – gum bleeding, epistaxis, ecchymosis.

CVS:

RS :

ABD:

CNS :

INVESTIGATIONS:

1. Complete Blood Count
2. Bleeding time / Clotting time
3. Urine Albumin, Sugar, Deposits including RBCs
4. Blood Sugar, urea, serum creatinine, electrolytes
5. LFT
6. Electrocardiogram
7. USG abdomen
8. 24hr Urinary protein if done
9. CT Brain for required cases.
10. Other investigations were taken based on the clinical status of the patient.
11. Autopsy findings of Kidney.

Hospital Course:

Date / Time: **ASV:** **C T:** **Others:**

Management: □ Specific (ASV) □ Conservative □ PD □ HD □ Both No. of sittings:

Outcome: □ Complete recovery □ Death

A SNAKE BITE PATIENT SHOWS CELLULITIS WITH FANG MARK

A SNAKE BITE PATIENT UNDERGOING PERITONEAL DIALYSIS

A SNAKE BITE PATIENT UNDERGOING HEMO DIALYSIS

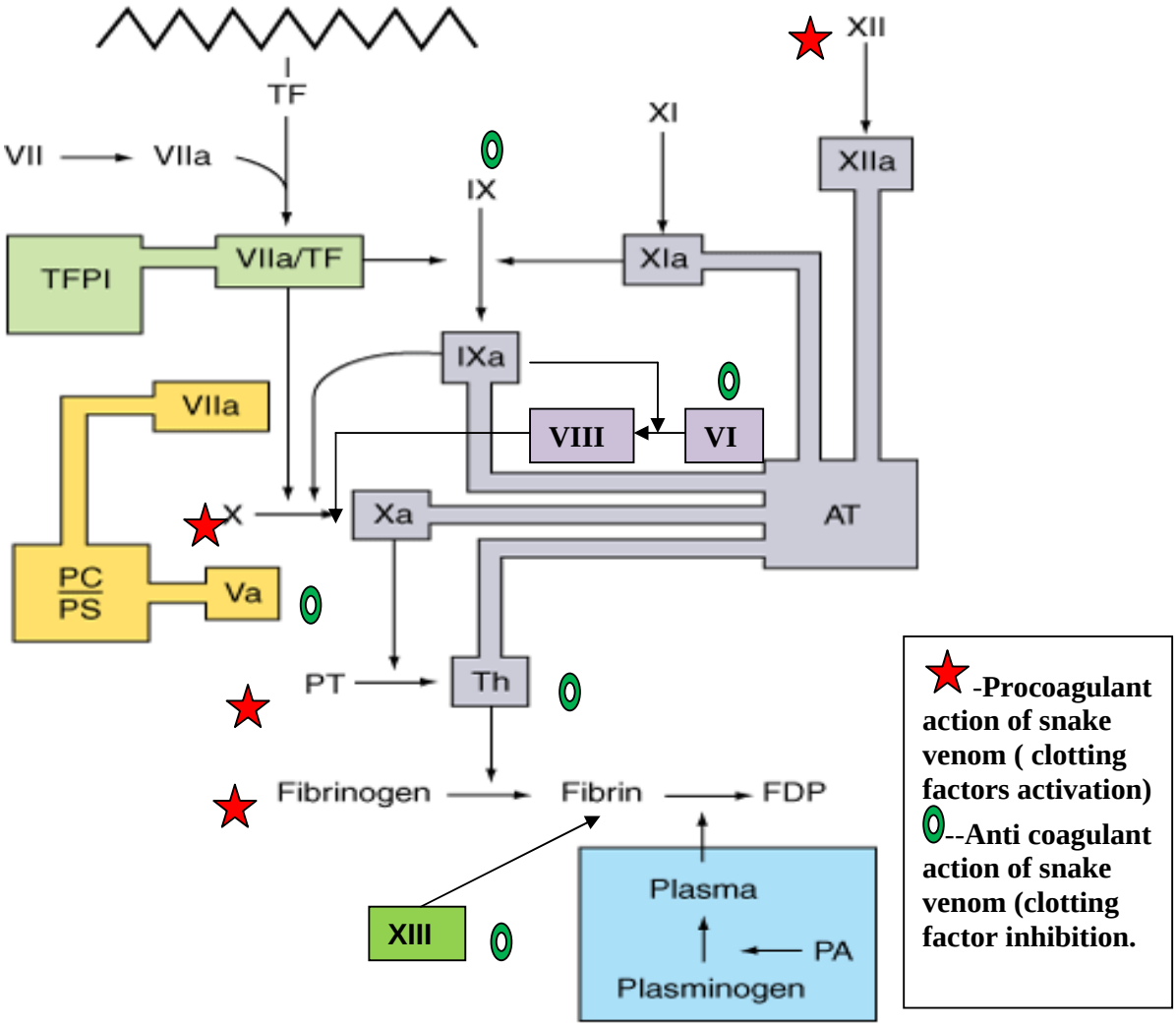
COBRA (NAGA PAMBU)

COMMON KRAIT (KATTU VIRIYAN)

RUSSELL VIPER(KANNADI VIRIYAN)

SAW SCALED VIPER (SURUTTAI PAMBU)

SNAKE VENOM AND THE COAGULATION PATHWAY



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